



Reversing the De-Evolution of Our Gut Flora to Combat Obesity and its Comorbidities

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Abstract

Obesity has become a global epidemic, resulting in an increase in obesity-related illnesses and an astounding estimate of 147 billion dollars for medically-related costs in the U.S. in 2008. According to the Harvard T.H. Chan School of Public Health, less than 15% of the U.S. population was obese in 1990. That percentage grew to over 25% in 2010 and in 2016, 69% of adults in the U.S. were overweight and 36% were obese. There are a number of genetic and environmental factors that can lead to obesity, but a decrease in the diversity of gut bacteria caused by antibiotics and emulsifiers has also been shown to be related to the increase in obesity. Antibiotics and emulsifiers were introduced commercially at roughly the same time (early to mid-1900s) and from that time, there began to be an increase in the prevalence of obesity and its comorbidities. An increase in the diversity of gut bacteria is needed to help combat obesity. Studies have shown that increasing the diversity of the microbiome leads to decreased gastrointestinal symptoms and lowered levels of obesity. Increasing the density and diversity of the gut bacteria is a natural way to combat obesity and improve overall health.

Keywords: Microbiome; Microbial diversity; Emulsifiers; Antibiotics; Obesity

Introduction

The diversity of our gut bacteria is becoming increasingly diminished and there is evidence that this decrease has been caused at least in part by the introduction of antibiotics and emulsifiers into the general population roughly at the same time. Emulsifiers began to be added into foods in the 1930's and antibiotics began to experience their golden era in the 1950's [1-3]. Beginning with the generation of people that were young during that era, we have seen a marked increase in mental illnesses, spectrum and autoimmune disorders, type II diabetes, heart disease and obesity (known collectively as 20th-century illnesses) [1,4,5].

Each person hosts bacteria on and inside of their body – this is referred to as the normal flora and the microorganisms in the gut are called the gut flora or microbiome. The gut can contain 100 trillion bacteria. Genetics has a large part to do with the composition of a person's gut flora but bacteria can also be introduced into a person's flora to help increase the diversity [6,7]. Beginning with the mode of birth (whether vaginal or caesarean) and then whether a baby is breastfed or bottle-fed, is given antibiotics, and what type of foods are consumed, the microbiome that each person develops is affected by many factors [8-10]. A person's microbiome is also affected by the people that he or she interacts with, most notably family members and cohabitants [11].

Each strain of healthy bacteria has a job to do and by increasing the variety of bacteria present, it is possible to increase the efficiency of the gut microbiome in order to make a person healthier because their gut is functioning more properly. When the bacterial composition has been compromised by outside factors such as taking antibiotics or eating foods containing emulsifiers, the result is a decreased gut flora

that does not function properly, causing a decline in overall health [12]. The gut flora has come to the forefront of medical research as its importance in immunology, digestive health, psychology, metabolism, and cardiovascular health have been realized but there is still much to be learned about the bacteria that share our bodies [11]. In an attempt to combat the growing epidemic of obesity, there are two ways that the diversity of gut bacteria could be increased: through consumption of probiotics and fecal transplants (bacteriotherapy) [6].

Discussion

An emulsifier is a substance that provides or enhances the stability of components that would otherwise separate when mixed; an example is how oil and water behave. Emulsifiers were initially added to cake batter to improve the texture, to make a lighter and softer cake [4]. It was quickly discovered that emulsifiers could extend the shelf life of baked goods, improve the quality of processed foods, and deliver a preferred mouthfeel or texture to foods [4]. Emulsifiers have been linked to gastrointestinal inflammation and bacterial translocation (bacteria migrating across the intestinal wall into the bloodstream) [13,14]. A study was performed on mice using emulsifiers. The mice that were given food with emulsifiers, specifically carboxymethylcellulose (CMC) and polysorbate-80, were more likely to become obese and develop metabolic disorders such as glucose intolerance and inflammatory bowel disease, even though the FDA has ruled that emulsifiers are "generally regarded as safe" [13,15]. Mice that were fed one-tenth of the amount of emulsifiers that the FDA has determined to be safe showed glucose intolerance and increased obesity [15].

A second finding of the murine emulsifier study was that when the colonic bacteria was analyzed from the mice that ate the food with commercial emulsifiers, they had less microbial diversity than the control mice and "the microbes had migrated closer to the cells lining

the gut" [15]. The significance of this migration is that when the microbes get too close to the intestinal lining, this creates a disturbance in the lining and results in leaky gut syndrome. Leaky gut syndrome is the cause for many health issues ranging from allergies and asthma to eczema, migraines, irritable bowel disease, fibromyalgia, rheumatoid arthritis and autoimmune diseases. Once the intestine becomes leaky, the bacteria can more easily cross the intestinal wall (translocation) and enter the bloodstream. Sato showed that persons with type II diabetes have gut bacteria in circulation, showing this translocation occurs in humans [16].

Antibiotic compounds have been used by mankind as early as the 4th century, but when penicillin was discovered, it quickly became the standard treatment for any infection [4]. This explosion of antibiotic use began in the 1950s and continues today. Antibiotics are typically inexpensive and a quick way to treat an infection; they are given prophylactically for surgery, dental procedures, and prescribed to treat infection. The downside to antibiotics is that they are "indiscriminant in their eradication of bacteria and can have a deleterious effect on the healthy bacteria in a person's body as the antibiotic works to eliminate the pathogenic bacteria" [17]. An antibiotic can decimate the microbiome. If probiotics are not taken concurrently with an antibiotic, the flora can be altered permanently [18]. As antibiotics became prevalent in the medical field, they also gained popularity in the agricultural world, being fed to animals to prevent infection and to enhance weight gain [19]. People have been unnecessarily exposed to antibiotics from food sources such as meat and plants to water sources and prescriptions [20].

As the use of antibiotics increased, their effect on the microbiome has progressively decreased the diversity of the gut flora. Yassour et al. showed (through RNA and whole-genome sequencing of the bacteria) that stool samples of babies that were given antibiotics exhibited a decrease in microbial diversity as well as an increase in antibiotic resistance [9]. Furthermore, at 36 months of age, children who had not been given antibiotics showed higher levels of microbial diversity and a more stable microbiome [9]. This study shows that antibiotics negatively impact the microbiome not only immediately after the antibiotic consumption but years later. Another significant find of Yassour's study was that while the density of a bacterial species may rebound post-antibiotic, the number of strains was diminished; the result of antibiotics is an overall decrease in microbial diversity [9]. A study of adults who were given antibiotics showed that immediately after antibiotic consumption, there was a sharp decrease in gut microbial diversity (through 16S rRNA tag pyrosequencing). The fecal bacteria of these same adults were tested at one year and again at four years post-antibiotic consumption and the results were an overall decrease in bacterial diversity. The most shocking result was that antibiotic resistance genes which appeared immediately following the antibiotic treatment were present in indigenous bacterial species four years later [21].

Decrease in the diversity of gut bacteria has been shown to have negative effects on the overall health of people and to cause obesity [5,12,22]. Less bacterial diversity has led to an alarming increase in health problems and diseases [5]. In addition to a decrease in diversity in the microbiome, there is also a decrease in the biodiversity of edible plants and animals [1]. Obesity has become a world-wide epidemic and the time frame of the increase in obesity correlates with the commercialization of both emulsifiers and antibiotics [1-3]. In an attempt to combat the increasing occurrence of obesity as well as its comorbidities such as insulin resistance, type II diabetes, liver disease,

and inflammatory bowel disease, it is necessary to increase the diversity of the gut flora. Fecal transplant or bacteriotherapy is the introduction a fecal sample from a healthy donor into the colon of a nonhealthy person [7]. Fecal transplants in humans started being performed in 1958 and were initially introduced as a treatment for *Clostridium difficile* infection but have begun to be investigated and used as treatment options for other gastrointestinal diseases and obesity [7]. Probiotic consumption is generally regarded as a safe treatment for gastrointestinal dysbiosis [23]. Clinical trials are showing that probiotics can reduce symptoms of irritable bowel syndrome and increase the density and diversity of the gut flora, and reduce the level of obesity [12, 23-25].

Conclusion

Obesity can lead to cardiovascular disease, type II diabetes, and other illnesses [24]. According to the CDC, the medical costs associated with obesity in the United States were estimated at \$147 million in 2008. It is imperative that we find effective means of combating the escalating obesity epidemic. Gastrointestinal inflammation, leaky gut syndrome, translocation of gut bacteria, and irritable bowel syndrome are shown to be caused by a decrease in the diversity of the gut flora [13-15,16]. These digestive tract abnormalities can lead to obesity [24]. Clinical implications of this research are that effective treatments for the reduction and prevention of obesity could be enhancing the density and diversity of the gut microbiome through probiotic supplementation and bacteriotherapy [1,7,12,23,25]. Treatments such as probiotic supplementation and bacteriotherapy are needed to reverse the obesity epidemic. As the incidence of obesity and its comorbidities continue to increase, so will the medically-related costs. Current treatments for obesity that include bariatric surgery, liposuction, and medications with undesirable and negative long-term side effects are not curbing the obesity epidemic. The need for alternative treatments is evident and fighting the obesity epidemic from the inside out by treating the gut flora could prove to be a desirable option.

Further study into the role of each strain of bacteria in the microbiome is needed in order to develop a probiotic that would deliver a maximal amalgamation of healthy bacteria. Another area of study that could augment this developing field would be to obtain fecal samples from indigenous populations to catalog and study the bacteria present in these samples for strains that have been exterminated in developed populations. If beneficial strains are discovered, they could be added into probiotics and bacteriotherapy samples as a way to increase the diversity of the gut microbiome to help reduce obesity and its comorbidities.

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